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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,744	03/25/2005	Noboru Maki	053466-0395	7902

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EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,744	MAKI ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4 and 6-21* is/are pending in the application.

4a) Of the above claim(s) *7-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,6 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 11, 2009, has been entered.

Claim Objection

2. Claim 4 recites: "An isolated HBV core-like particle comprising an isolated HBV precore protein, wherein the *N*-terminus of the precore protein is at postition -28 and the *C*-terminus is at a position from 150 to 154, as set forth in SEQ ID NO: 1, further not comprising HBV DNA therein". Claim 4 is objected to because of the following informalities: (1) "postition -28" is mis-spelt, should be "position -28". (2) It is noted that in the sequence listing, SEQ ID NO: 1 starts at position 1 and ends at position 178. It is not clear how "*N*-terminus of the precore protein is at position -28 and the *C*-terminus is at a position from 150 to 154" is located in SEQ ID NO: 1. (3) "An isolated HBV core-like particle comprising an isolated HBV precore protein" is confusing because it is not clear if the precore protein is "isolated" from the HBV-core-like particle, or is composed of an HBV-core-like particle. Applicant is suggested to delete "isolate" from "an isolated HBV precore protein" for clarity. Appropriate corrections are required.

4. For the purpose of the examination, Claim 4 is interpreted as "An isolated HBV core-like particle comprising an ~~isolated~~ HBV precore protein, wherein the HBV precore protein comprises the sequence of SEQ ID NO: 1, and further not comprises HBV DNA therein".

Claim Rejections - 35 USC § 112, first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. **(Prior rejection-withdrawn)** The rejection of Claim 4 under 112, 1st paragraph, for failing to comply with written description requirement, is withdrawn in view of the amendment to the claim.

7. **(Prior rejection-withdrawn)** The rejection of Claims 4 and 6 under 35 U.S.C. 112, first paragraph for failing to comply with the enablement requirement (scope of enablement), **is withdrawn** in view of the amendment to the claims. The rejection of Claims 1 and 5 is moot in view of the cancellation of the claims.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. **(Prior rejection-withdrawn)** The rejection of Claim 21 under 35 U.S.C. 102(b), as being anticipated by Takahashi (J. Immunology, 147(9): 3156-3160, 1991) **is withdrawn** in view of the amendment to the claim.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. **(Prior rejection-withdrawn)** The rejection of Claims 1-4 under 35 U.S.C. 103(a) as being unpatentable over Takahashi (J. Immunology, 147(9):3156-3160, 1991, cited in IDS), in view of Kobayash, **is withdrawn** in view of the amendment to the claim. The rejection of Claims 1-3 is moot in view of the cancellation of the claims.

102/103 Rejection

12. **(New rejection)** Claims 4, 6 and 12 are rejected under 35 U.S.C. § 102(b) as anticipated by or, alternatively, under 35 U.S.C. § 103 as obvious over Sakamoto (Laboratory Investigation, 48, 678-682, 1983, cited in IDS), as evidenced by Ou (Virology 174, 185-191, 1990) and Miyanohara (J. Virology, 59(1):176-180).

13. Claim 4 is interpreted as "An isolated HBV core-like particle comprising an HBV precore protein, wherein the HBV precore protein comprises the sequence of SEQ ID NO: 1, and further not comprises HBV DNA therein" (See Para 4 above).

14. Claim construction: The specification provides the following teaching regarding the claimed HBV core-like particle, which is also called as "the HBV core related antigen" and "p22 antigen" in the specification, and "HBcrAg" in Figures: **(1)** the claimed HBV core-like particle, exists in the **serum of HBV patient,** see e.g. [0041]. **(2)** It is isolated from **the serum of HBV patient** by sucrose density gradient centrifugation; see Para [0041] and [0042]. The HBV core

related antigen forms incomplete virus particle, see e.g. [0047]. (3) The sequence analysis of the HBV core-related antigen (p22 antigen) discloses that it is a HBV precore protein comprising 178 amino acids as set forth in SEQ ID NO: 1, Para [0045].

15. Furthermore, the specification teaches that the HBV precore protein was known to be a precursor of HBe, and HBc (HBV core antigen), which known to form a core-like particle, see Fig. 1 and Para [0010]. The specification Para [0012] acknowledges: "it has been reported that, among Dane particles, there are some empty particles containing no HBV-DNA (Sakamoto *et al.*, Laboratory Investigation, 48, 678-682, 1983)..., but the HBV protein constituting the particle has not been analyzed in detail".

16. Sakamoto teaches that empty Dane particles (without DNA) of HBV present in HBV patient, in addition to full particles (with DNA), see Title. Naked core particles (without DNA) were isolated when the serum of a patient was fractionated by sucrose density gradient centrifugation, see whole document, and Abstract. The isolated full and empty HBV core particles are shown in Figure 1. Sakamoto teaches that most Dane particles in patents' serum do not contain viral DNA (see Para 2, right col. p. 681). However, Sakamoto does not teach the sequence of the isolated empty core particle.

17. The empty Dana-particles (without DNA), taught by Sakamoto appear to be the same product, or an obvious variant of the claimed "isolated HBV core-like particle comprising an isolated HBV precore protein, ...further not comprising DNA therein", given that (1) they are all naturally occurring particles existing in HBV patients; (2) they can be isolated from serum of HBV patient by same process of sucrose density gradient centrifugation; and (3) HBV precore protein is known to be capable of forming HBV core-like particles, see Ou and Miyanohara

(whole document) as evidence. Both teach that HBV precore protein has property of forming core-like particle when it is expressed in mammalian or yeast cells.

18. Since the empty Dana-particles (without DNA), taught by Sakamoto appear to be the claimed "isolated HBV core-like particle comprising an HBV precore protein, the claimed sequence of SEQ ID NO:1 must be inherently disclosed in Sakamoto. Thus, the subject matter of Claims 4, 6 and 12 are anticipated by or, alternatively, are obvious over Sakamoto. Where applicant claims a composition in terms of a characteristic not explicitly disclosed by the reference, a 102/103 rejection is proper (MPEP 2112).

19. It's the Applicant's burden under the circumstances presented herein to establish that a prior art product does not necessarily possess the characteristics of the claimed product when the prior art and claimed products are identical or substantially identical, See citation in In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977) as follows:

Where, as here, the claimed and prior art products are identical or substantially identical, **or are produced by identical or substantially identical processes**, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. . . . Whether the rejection is based on `inherency' under 35 U.S.C. § 102, on `prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted].

While "indirect comparisons, based on established scientific principles, can validly be applied to distinguish a claimed chemical process or product from that disclosed in the prior art," In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 432 (CCPA 1977), the comparisons must be scientifically valid.

Remarks

20. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Examiner, Art Unit 1648